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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/697,703	10/31/2003	H. William Bosch	029318-0973	8369

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ELAN DRUG DELIVERY, INC.
C/O FOLEY & LARDNER LLP
3000 K STREET, N.W.
SUITE 500
WASHINGTON, DC 20007-5109

EXAMINER	
MAHYERA, TRISTAN J	

ART UNIT	PAPER NUMBER
1609	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/697,703	BOSCH ET AL.	
	Examiner	Art Unit	
	Tristan J. Mahyera	1609	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 March 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-95* is/are pending in the application.

4a) Of the above claim(s) *32-35,39,41-43 and 45-95* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-31,36-38,40 and 44* is/are rejected.

7)☒ Claim(s) *27 and 37* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *See Continuation Sheet*.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :03/26/2007, 12/20/2006, 10/13/2006, 07/12/2006, 12/29/2004, 04/01/2004.

DETAILED ACTION

Priority

1. Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

Continuation 09/572,961 and Continuation-in-Part 10/276,400 do not provide support for nimesulide or compositions comprising nimesulide. While the parent documents teach the general term NSAIDs, it does not explicitly teach nimesulide, thus the instant application is not granted the benefit of priority. Therefore, the effective priority date is 10/31/2003. If Applicant disagrees, they are encouraged to point to a specific page and line where evidence of such support is provided.

Restriction/Election

2. Applicant's response dated February 26, 2007 in response to the Restriction/Election is acknowledged. Furthermore, the Examiner initiated telephone interview to clarify and request species election compliance is summarized on Form PTO-413B. Faxed response from Applicant was received August 21, 2007 specifying "codeine" as the elected species #5.

In Applicant's response to the restriction requirement, Applicant elected Group I, claims 1-44, drawn to a nimesulide composition without traverse. Applicant further elected five species:

Species election #1: Applicant elected "crystalline"

Species election #2: Applicant elected "oral"

Species election #3: Applicant elected "tablets"

Species election #4: Applicant elected a "random copolymer of vinyl acetate and vinyl pyrrolidone" (Plasdone® S-630).

Species election #5: Applicant elected "codeine" by fax received Aug 21, 2007.

Pursuant to Applicants elections, Group II and Group III, Claims 45-95, are withdrawn as directed to non-elected inventions. Claims 32-35, directed to a liquid dosage form, are withdrawn as directed to non-elected dosage form. Claims 39 and 41-43, directed to non-nimesulide active agents, are withdrawn as directed to non-elected non-nimesulide active agent.

Therefore, Claims 1-31, 36-38, 40 and 44 are examined on the merits as reading on the elected species.

Claim Objections

3. Claim 27 is objected to because of the following informalities: "that" should be "then". Appropriate correction is required.

Claim Rejections

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-31, 36, 37, 38, 40 and 44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6. Claim 1 uses the terms "less than" and "about" to describe the effective particle size, which does not particularly point out and distinctly claim the subject matter. Taking into consideration Applicant's definition of "about" as plus or minus 10% (see page 10 and 11 paragraph [0030]) which gives a range of 1800nm to 2200nm, the use of "less than" renders the claim indefinite because it is unclear if Applicant is trying to claim less than 1800nm, less than 2200nm or less than somewhere within the range 1800nm to 2200nm, such as the stated 2000nm.

7. Claim 13 recites trademarks or trade names, which without the underlying product causes confusion by not distinctly claiming the exact surface stabilizer compound or composition. The terms POLYQUAT 10™, MIRAPOL™ and ALKAQUAT™ are used as limitations in Claim 13. Trademarks or trade names identify a source of goods, and not the goods themselves. Thus a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. If the trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of the 35

U.S.C. 112, second paragraph. Ex parte Simpson, 218 USPQ 1020 (Bd. App. 1982). See MPEP 2173.05(u).

8. The term "significantly" in claim 22 is a relative term that renders the claim indefinite. The term "significantly" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably appraised of the scope of the invention. Claims 22 makes a comparison between the fed absorption levels and the fasting absorption levels but does not establishing what are considered "significantly different absorption levels" between the two conditions. This problem arises because the metes and bounds of when "significantly different absorption levels" become insignificant cannot be determined.

9. Claim 37 is internally inconsistent because its preamble recites a method, yet it depends from a claim drawn to a composition. Applicant is required to cancel the claim, amend the claim to place the claim in proper dependent form or rewrite the claim in independent form.

10. All remaining Claims are rejected as depending from rejected Claim 1.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the

applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

12. Claims 1-14 and 27-31 are rejected under 35 U.S.C. 102(e) as being anticipated by OLIVIERI et al (WO 2005/000273).

13. OLIVIERI et al. describes how to obtain a carrier copolymer of N-vinyl-2-pyrrolidone/vinyl acetate (NVP/VA) and active substance, specifically nimesulide, supported in said carrier. Ratios of carrier NVP/VA to nimesulide are preferably disclosed in the range of 200:1 to 1:10 and more preferably between 100:1 to 1:5 and specifically 10:1 to 0.5:1. See page 4 lines 23-26, Tables 1-4 and Examples 1-4. Particle size of both nimesulide and NVP/VA are independently disclosed as between 0.01 microns (10nm) and 1,000 microns (1,000,000nm) and specifically between 0.1 microns (100nm) and 200 microns (200,000nm). See page 4 lines 2-5. The invention can subsequently be sieved or used directly in the preparation of the desired pharmaceutical form, specifically a tablet. See page 4 lines 29-31, and page 6 line 26 to page 7 line 3 and claim 14. Additionally, nimesulide and carrier NVP/VA were combined with non-nimesulide agents and additional excipients, stabilizers or carriers. See Table 1 and 6, page 10 lines 31-33, page 5 line 5 to page 6 line 9 and claim 15. It is also disclosed that the use of NVP/VA as a carrier results in improvements of the crystalline structure of the active drugs, specifically nimesulide. See page 3 lines 15-20 and Table 1.

14. Instant Claims 1, 3, 27-31 are directed to an effective particle size of nimesulide or additional nimesulide composition. Claim 1, 28 and 30 state "less than about

2000nm"; Claim 3, 29, 31 state "less than 1900nm"; Claim 27 states a different size than the nimesulide composition of Claim 1. OLIVIERI et al. describes a particle size of both nimesulide and/or NVP/VA as between 0.01 microns (10nm) and 1000 microns (1,000,000nm) and specifically between 0.1 microns (100nm) and 200 microns (200,000nm). See page 4 lines 2-5. Therefore, OLIVIERI et al. anticipates Instant Claims 1, 3, 27-31.

15. Instant Claim 2 is directed to the crystalline phase of nimesulide. OLIVIERI et al. describes that the use of NVP/VA as a carrier results in improvements of the crystalline structure of the active drugs, specifically nimesulide. See page 3 lines 15-20 and Table 1. Therefore, OLIVIERI et al. anticipates Instant Claim 2.

16. Instant Claims 4–6 are directed to oral administration of the composition and tablets as the dosage form and further excipients or carriers. OLIVIERI et al. describes preparation of the desired oral pharmaceutical form, specifically a tablet. See page 4 lines 29-31, and page 6 line 26 to page 7 line 3 and claim 14. Therefore, OLIVIERI et al. anticipates Instant Claims 4 and 5.

17. Instant Claims 7-14 are directed to nimesulide and at least one surface stabilizer. OLIVIERI et al. describes nimesulide with stabilizer NVP/VA and the further combination with non-nimesulide agents and additional excipients, stabilizers or carriers. See Table 1 and 6, page 10 lines 31-33, page 5 line 5 to page 6 line 9 and claim 15. Therefore, OLIVIERI et al. anticipates Instant Claims 7-14.

Claim Rejections - 35 USC § 103

18. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

19. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Examiner has considered the factual inquires set forth in *Graham* **v.** *John Deere Co.*

20. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

21. Claims 2 and 15-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over OLIVIERI et al. (WO 2005/000273) in view of SINGH et al. (Analytical Profiles of

Drug Substances and Excipients, Volume 28, 2001, p197-249) and in view of BOSCH et al. (US 5,510,118).

22. Instant Claims 2 and 15-26 are directed to physical properties and pharmacokinetics of nimesulide. OLIVIERI et al. describes the use of nimesulide in a composition and that the use of NVP/VA improves the crystalline structure of the nimesulide, however, it does not give data related to Tmax, Cmax and AUC of nimesulide, but motivates one to improve absorption properties, which Tmax, Cmax and AUC are indicators. SINGH et al. describes the pharmacokinetic and bioavailability properties of nimesulide (see section 7) and BOSCH et al. teaches that bioavailability is the degree to which a drug becomes available to the target tissue after administration (see column 1 lines 11-12) and the rate of dissolution of a particular drug can increase with increasing surface area, i.e. decreasing particle size (see column 1 lines 25-27). A person skilled in the art preparing pharmaceutical compositions would know that decreasing the size of a compound would increase its bioavailability, increase the AUC, increase the Cmax and decrease the Tmax. Thus, it would have been obvious to such a person skilled in the art at the time of the instant invention to practice with nanoparticles of nimesulide, resulting in the practice of the instantly claimed invention with a reasonable expectation of success.

23. Instant Claims 37, 38 and 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over OLIVIERI et al. (WO 2005/000273) in view of SINGH et al. (Analytical Profiles of Drug Substances and Excipients, Volume 28, 2001, p197-249) and in view of MERCK (The Merck Index 12th ed. Merck & Co. 1996, codeine, p416-417).

24. Instant Claims 36 - 38 and 40 are directed to the addition of a non-nimesulide active agent, such as analgesics, specifically codeine. OLIVIERI et al. teaches using nimesulide and NVP/VA in a pharmaceutical composition, it further teaches using analgesics as the active substance in the composition, but does not teach adding additional specific analgesics to the composition. See Table 1 and 6, page 10 lines 31-33, page 5 line 5 to page 6 line 9 and claim 15. SINGH et al. teaches it is well known in the art that nimesulide has anti-inflammatory and analgesic properties. See section 1.5. It is also well known in the art that codeine has analgesic properties as shown in MERCK. Furthermore, "It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980). Thus, the addition of codeine, an analgesic, would be obvious to someone of skill in the art at the time of the invention because nimesulide also has known analgesic properties, resulting in the practice of the instantly claimed invention with a reasonable expectation of success.

25. Instant Claim 44 is rejected under 35 U.S.C. 103(a) as being unpatentable over OLIVIERI et al. (WO 2005/000273) in view of BUHL et al. (US 5776563).

26. Claim 44 is directed to sterile filtration of the composition of claim 1. OLIVIERI et al. describes compositions of nimesulide and NVP/VA, but does not specify the method of sterilization. OLIVIERI et al. further teaches a pharmaceutical composition an

ordinary skilled artisan would be motivated to sterilize because as common sense would suggest, it is desirable to ensure that a composition administered to a subject is free of microorganisms. See page 6 lines 26-28. BUHL et al. teaches that pharmaceutical compositions can be sterilized by conventional sterilization techniques or may be sterile filtered. See column 4 lines 7-26. Therefore, it would have been obvious to someone of ordinary skill in the art at the time of the instant invention to sterile filter the composition of instant Claim 1, resulting in the practice of the instantly claimed invention with a reasonable expectation of success.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tristan J. Mahyera whose telephone number is 571-270-1562. The examiner can normally be reached on Monday through Thursday 9am-4pm EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic

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/TJM/

Ardin H. Marschel 9/1/07
ARDIN H. MARSCHEL
SUPERVISORY PATENT EXAMINER